

In the Claims

Please cancel Claims 2, 3, 4, 7 and 13-44 without prejudice.

Please amend Claims 1, 5, 6, 8, 45 and 52 as follows:

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1. (Amended) An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 [or portion of said receptor], wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine [ligand] to [the] said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof binds the amino-terminal domain of said receptor.

~~2.2~~
 (Amended) An antibody or antigen-binding fragment thereof according to Claim [4] 1 wherein said antibody or antigen-binding fragment binds a [the] portion of the amino-terminal domain which is from about amino acid 1 to about amino acid 30 of said receptor.

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- ~~3.2~~
 (Amended) An antibody or antigen-binding fragment thereof according to Claim 1 wherein the antibody is selected from the group consisting of:
- a) monoclonal antibody 1D9;
 - b) an antibody having [an] the epitopic specificity [which is the same as or similar to that] of 1D9;
 - c) [an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor;
 - d)] monoclonal antibody ~~8G2~~;
 - [e)] d) an antibody having [an] the epitopic specificity [which is the same as or similar to that] of 8G2; and
 - [f) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2; and
 - g)] e) antigen-binding fragments of any one of (a) through [(f)] (d) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.
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8.

(Amended) An antibody or antigen-binding fragment thereof according to Claim [7] 1 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

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(Amended) A composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 [or portion of said receptor], wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine [ligand] to [the] said receptor[,], and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof binds the amino-terminal domain of said receptor, and an optional physiologically acceptable vehicle.

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52.

(Amended) A method of treating a CC-chemokine receptor 2-mediated disorder in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 [or portion thereof], wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof binds the amino-terminal domain of said receptor.

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Please add new Claims 53-106 as follows:

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A method according to Claim ~~52~~ ⁶, wherein said CC-chemokine receptor 2-mediated disorder is an autoimmune disorder.

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A method according to Claim ~~53~~ ⁷, wherein the autoimmune disorder is selected from the group consisting of multiple sclerosis and rheumatoid arthritis.

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55. A method according to Claim 54, wherein the autoimmune disorder is multiple sclerosis.
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56. A method according to Claim 52, wherein the CC-chemokine receptor 2-mediated disorder is selected from the group consisting of atherogenesis and atherosclerosis.
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57. An antibody or antigen-binding fragment according to Claim 1, wherein said antibody or fragment is a monoclonal antibody or fragment thereof.
58. An antibody or antigen-binding fragment according to Claim 1, wherein said antibody or fragment is a chimeric antibody or fragment thereof.
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59. An antibody or antigen-binding fragment according to Claim 1, wherein said antibody or fragment is a human antibody or fragment thereof.
60. An antibody or antigen-binding fragment according to Claim 1, wherein said antibody or fragment is a humanized antibody or fragment thereof.
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61. An antibody or antigen-binding fragment according to Claim 1, wherein said antigen-binding fragment is selected from the group consisting of an Fv fragment, an Fab fragment, an Fab' fragment and an F(ab')₂ fragment.
62. A humanized antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said humanized antibody comprises one or more antigen-binding regions of monoclonal antibody 1D9.
63. A humanized antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said humanized antibody comprises one or more complementarity-determining regions of monoclonal antibody 1D9.

64. A humanized antibody or antigen binding fragment thereof according to Claim 63, which comprises six complementarity-determining regions of monoclonal antibody 1D9.
65. A composition comprising a humanized 1D9 antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2 and an optional physiologically acceptable vehicle.
66. A pharmaceutical composition comprising a humanized 1D9 antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2 and a physiologically acceptable vehicle.
67. A recombinant antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said recombinant antibody comprises one or more complementarity-determining regions of monoclonal antibody 1D9.
68. A recombinant antibody or antigen-binding fragment according to Claim 67, wherein said recombinant antibody comprises six complementarity-determining regions of monoclonal antibody 1D9.
69. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof can compete with monoclonal antibody 1D9 for binding to said receptor.
70. An antibody or antigen-binding fragment thereof according to Claim 69, wherein said mammalian CC-chemokine receptor 2 is a human CC-chemokine receptor 2.

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An antibody or antigen-binding fragment thereof according to Claim ~~69~~, wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

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A composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof can compete with monoclonal antibody 1D9 for binding to said receptor, and an optional physiologically acceptable vehicle.

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A pharmaceutical composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof can compete with monoclonal antibody 1D9 for binding to said receptor, and a physiologically acceptable vehicle.

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An antibody or antigen-binding fragment according to Claim ~~69~~, wherein said antibody or fragment is a monoclonal antibody or fragment thereof.

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75. An antibody or antigen-binding fragment according to Claim 69, wherein said antibody or fragment is a chimeric antibody or fragment thereof.

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An antibody or antigen-binding fragment according to Claim ~~69~~, wherein said antibody or fragment is a human antibody or fragment thereof.

77. An antibody or antigen-binding fragment according to Claim 69, wherein said antibody or fragment is a humanized antibody or fragment thereof.

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78. An antibody or antigen-binding fragment according to Claim 69, wherein said antigen-binding fragment is selected from the group consisting of an Fv fragment, an Fab fragment, an Fab' fragment and an F(ab')₂ fragment.

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79. A composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof can compete with monoclonal antibody 8G2 for binding to said receptor, and an optional physiologically acceptable vehicle.

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80. A pharmaceutical composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof can compete with monoclonal antibody 8G2 for binding to said receptor, and a physiologically acceptable vehicle.

81. A humanized antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said humanized antibody comprises one or more antigen-binding regions of monoclonal antibody 8G2.

82. A humanized antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said humanized antibody comprises one or more complementarity-determining regions of monoclonal antibody 8G2.

83. A humanized antibody or antigen binding fragment thereof according to Claim 82, which comprises six complementarity-determining regions of monoclonal antibody 8G2.
84. A composition comprising a humanized 8G2 antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2 and an optional physiologically acceptable vehicle.
85. A pharmaceutical composition comprising a humanized 8G2 antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2 and a physiologically acceptable vehicle.
86. A recombinant antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said recombinant antibody comprises one or more complementarity-determining regions of monoclonal antibody 8G2.
- 2.1.24
87. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof can compete with monoclonal antibody 8G2 for binding to said receptor.
- 2.1.25
88. An antibody or antigen-binding fragment thereof according to Claim 87, wherein said mammalian CC-chemokine receptor 2 is a human CC-chemokine receptor 2.
- 2.1.26
89. An antibody or antigen-binding fragment thereof according to Claim 87, wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

90. A recombinant antibody or antigen-binding fragment according to Claim 86, wherein said recombinant antibody comprises six complementarity-determining regions of monoclonal antibody 8G2.

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91. An antibody or antigen-binding fragment according to Claim 87, wherein said antibody or fragment is a monoclonal antibody or fragment thereof.

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92. An antibody or antigen-binding fragment according to Claim 87, wherein said antibody or fragment is a chimeric antibody or fragment thereof.

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93. An antibody or antigen-binding fragment according to Claim 87, wherein said antibody or fragment is a human antibody or fragment thereof.

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94. An antibody or antigen-binding fragment according to Claim 87, wherein said antibody or fragment is a humanized antibody or fragment thereof.

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95. An antibody or antigen-binding fragment according to Claim 87, wherein said antigen-binding fragment is selected from the group consisting of an Fv fragment, an Fab fragment, an Fab' fragment and an F(ab')₂ fragment.

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96. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor and inhibits one or more functions associated with binding of the ligand to the receptor at a concentration of less than about 10 µg/ml.

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97. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor and inhibits one or more

functions associated with binding of the ligand to the receptor at a concentration of less than about 0.1 $\mu\text{g/ml}$.

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98. An antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof binds the amino-terminal domain of said receptor.

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99. An antibody or antigen-binding fragment according to Claim 98, wherein said antibody or fragment is a monoclonal antibody or fragment thereof.

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100. An antibody or antigen-binding fragment according to Claim 98, wherein said antibody or fragment is a chimeric antibody or fragment thereof.

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101. An antibody or antigen-binding fragment according to Claim 98, wherein said antibody or fragment is a human antibody or fragment thereof.

102. An antibody or antigen-binding fragment according to Claim 98, wherein said antibody or fragment is a humanized antibody or fragment thereof.

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103. An antibody or antigen-binding fragment thereof according to Claim 98, wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

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104. A pharmaceutical composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the

chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof binds the amino-terminal domain of said receptor, and a physiologically acceptable vehicle.

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105.

A composition comprising an antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof binds to the amino-terminal domain of said receptor, and an optional physiologically acceptable vehicle.

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106.

A pharmaceutical composition comprising an antibody or antigen-binding fragment thereof which binds to a human CC-chemokine receptor 2, wherein said antibody or antigen-binding fragment thereof inhibits binding of a chemokine to said receptor and inhibits one or more functions associated with binding of the chemokine to said receptor, and wherein said antibody or antigen-binding fragment thereof binds to the amino-terminal domain of said receptor, and a physiologically acceptable vehicle.

REMARKS

Claim Amendments

Claims 2, 3, 4, 7 and 13-44 have been cancelled without prejudice.

Claims 1, 5, 6, 8, 45 and 52 have been amended.

Claims 1, 45 and 52 have been amended to recite that the antibody or antigen-binding fragment thereof inhibits binding of a chemokine to the receptor. Support for this amendment can be found throughout the Specification, for example, at page 4, line 5.

Claims 1, 45 and 52 have also been amended to recite that the antibody or antigen-binding fragment thereof inhibits one or more functions associated with binding of the

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